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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/705,300	11/10/2003	David H. Parma	NEX40CUSDC2	8392

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EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/705,300	PARMA ET AL.	
	Examiner	Art Unit	
	Dana Shin	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *65,66,68-70 and 72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *65,66,68-70 and 72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5-23-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

This Office action is in response to the communications filed on May 23, 2007.

Currently, claims 65-66, 68-70, and 72 are pending. Applicants have cancelled claims 67 and 71.

The following rejections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) remains denied for claim 68 since applicant has failed to provide adequate support for prior disclosure of SEQ ID NO:206 in applications filed prior to PCT/US96/09455.

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Rejections.

Claim Rejections - 35 USC § 112

Claims 65-66, 68-70, and 72 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for the reasons of record as set forth in the Office action mailed on November 24, 2006 and for the reasons stated below.

Applicant's arguments filed on May 23, 2007 have been fully considered but they are not persuasive. Applicant argues that many of the Examples in the specification were performed with SEQ ID NO:185 and SEQ ID NO:206 and therefore applicant provided sufficient direction as to how to identify nucleic acid ligands with desired activity and stability, which therefore mitigates the unpredictability formerly experienced by those practicing in the nucleic acid ligand field. Applicant's argument is correct in that the specification provides several Examples comprising SEQ ID NO:185 and SEQ ID NO:206; however, all of the Examples pertaining to SEQ ID NO:185 and SEQ ID NO:206 were performed *in vitro*. Applicant's statement that the applicant's SELEX method mitigates the "unpredictability formerly experienced by those practicing in the nucleic acid ligand field" may indeed apply to *in vitro* methods; however, there is no suggestion that the applicant's method would in fact lessen the unpredictability of SELEX-designed aptamers in a mammal *in vivo* with a resultant treatment effect for platelet disorder or lymphocyte trafficking disorder in the mammal. Applicant further contends that the specification demonstrates "proof of concept" with animal studies by performing the lymphocyte trafficking experiments. Although the specification provides animal studies, the two tested aptamers are neither of the claimed SEQ ID NOs. Moreover, the animal studies do not reflect a treatment

method for a lectin-mediated inflammation or a lymphocyte "tracking"[1] disorder or a platelet disorder; rather, they merely demonstrate that the two tested aptamers reduce the number of lymphocytes in the peripheral and mesenteric lymph nodes. Note that conception is not achieved until reduction to practice has occurred, regardless of the complexity of simplicity of the method of treating a mammal suffering from inflammation, lymphocyte trafficking disorder, or platelet disorder. For an actual reduction to practice, the invention must have been sufficiently tested to demonstrate that it will work for its intended purpose. See, for example, *Scott v. Finney*, 34 F.3d 1058, 1062, 32 USPQ2d 1115, 1118-19 (Fed. Cir. 1994). Emphasis added by examiner.

Applicant further argues that the claimed treatment methods were fully enabled as of the earliest filing date sought in the instant application, which is the year of 1995 or 1996. The unpredictability of DNA-based therapeutics at the time of filing as well as in the 21st century was stated at length in the Office action mailed on November 24, 2006. In order to overcome the art-recognized unpredictability of nucleic acid-based drugs (e.g., instantly claimed nucleic acid ligands), the specification must provide sufficient guidelines so as to produce the claimed therapeutic or treatment effect when the instantly claimed methods are practiced by one of ordinary skill in the art. As stated above, the instant specification is completely silent about any therapeutic or treatment effect in a mammal that is administered a nucleic acid ligand comprising SEQ ID NO:185 or 206. Furthermore, the advent of 96-mer oligodeoxyribonucleotides that act as nucleic acid ligands dates to 1992, as first taught by Bock et al.'s reference (*Nature,* February 6, 1992, 355:564-566, also applicant's citation). Bock et al. teach that single stranded 96-mer

[1] Claim 69 recites "lymphocyte tracking disorder" in line 2. It appears that the word "tracking" should be "trafficking" in view of the content of the specification and applicant's arguments filed on May 23, 2007. Clarification or correction is required.

DNA aptamers selected through putative SELEX methodology are able to bind to human thrombin *in vitro* and inhibit thrombin. Further, it is clear that using thrombin DNA aptamers for *in vivo* use in a mammal was far from being fully enabled, let alone feasible, as Bock et al. state "our long-term interest being to develop diagnostics and therapeutic agents." See page 566. Similarly, the 1996 reference of Wiegand et al. (*The Journal of Immunology,* 1996, 157:221-230) also teaches that "oligonucleotide-based compounds (referring to DNA aptamers identified via the SELEX method) have the potential to become a new class of potent therapeutic agents" on page 229. The teachings of the prior art therefore indicate that the use of DNA aptamers as therapeutic agents was "envisioned" at the time the instantly claimed invention was made; however, the "practical" use of DNA aptamers as therapeutic agents for treating a disorder was far from being solidly established as of the year of 1995 or 1996.

This lack of *in vivo* therapeutic effects of DNA aptamers during the early 1990's is further corroborated by the 1995 review article by Stull et al. (*Pharmaceutical Research,* 1995, 12:465-483, citation of record). The review article clearly teaches insufficient knowledge in the DNA aptamer art as of 1995, as it states "To date, only a few instances of oligonucleotide aptamers displaying biological effects have been reported." See page 466. Furthermore, with regard to the delivery obstacles prevalent in nucleic acids, it clearly teaches that "Cationic liposomes are effective for in vitro delivery of nucleic acid drugs and for in vivo gene transfer but to date have not been found useful for delivery of the low molecular weight nucleic acid drugs described in this review....the delivery and entry of nucleic acid drugs into the target site remains a major obstacle to the successful introduction of this aspect of the molecular biology evolution into a clinical setting." See pages 477-478. Emphasis added by examiner.

In light of the above, it is concluded that applicant's own disclosure fails to teach such level of confidence that any one of ordinary skill in the art can, without undue experimentation, use the inventor's nucleic acid ligands for their intended purpose: treatment of a platelet disorder, inflammation, and leukocyte trafficking disorder. Accordingly, claims 65-66, 68-70, and 72 remain rejected for failing to comply with the enablement requirement commensurate in scope with the claimed invention.

Double Patenting

Claims 65-66, 68-70, and 72 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 and 6-7 of U.S. Patent No. 6,544,959 B1. Applicant has not filed a terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) in order to overcome the nonstatutory obviousness-type double patenting rejection. Accordingly, this rejection is maintained.

New Rejections Necessitated by Amendments

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 66, 68, 70, and 72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 66 and 68 recite the limitation "said nucleic acid ligand to a lectin" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim because claim 65 is currently amended to recite a "nucleic acid ligand to P-selectin".

Claims 70 and 72 recite the limitation "said nucleic acid ligand to a lectin" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim because claim 65 is currently amended to recite a "nucleic acid ligand to L-selectin".

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

/J. E. Angell/
Primary Examiner
AU 1635